

CLAIMS

What is claimed is:

1. A peptide comprising a peptide derivative of the HJ loop of a serine/threonine
5 kinase, wherein:
 - a) said peptide has between about five and about twenty amino acids or amino acid analogs;
 - b) said peptide modulates activity of the serine/threonine kinase; and
 - c) said peptide is cyclic.
- 10 2. A peptide comprising a peptide derivative of the HJ loop of a serine/threonine kinase, wherein:
 - a) said peptide has between about five and about twenty amino acids or amino acid analogs;
 - b) said peptide modulates activity of the serine/threonine kinase; and
 - 15 c) said peptide has an N-terminus and a C-terminus which are unsubstituted.
3. A peptide which is an amino acid sequence or a subsequence of an HJ loop of a serine/threonine kinase, with the proviso that any one amino acid in the
20 sequence of the peptide derivative can vary, being any amino acid or analog thereof.
4. A peptide comprising a peptide derivative of the HJ loop of a serine/threonine kinase, wherein:
 - a) said peptide has between about five and about twenty amino acids or amino acid analogs;
 - 25 b) said peptide modulates activity of the serine/threonine kinase; and

- c) the serine/threonine kinase is member of a serine/threonine kinase family selected from the group of families consisting of Raf, mitogen-activated protein kinases (MAP kinases), G protein-coupled receptor kinases, or the serine/threonine kinase is selected from the group consisting of protein kinase C, cyclic AMP dependent kinase, calmodulin dependent kinase, cyclic GMP dependent protein kinase, Akt/PKB and GSK3.
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5. The peptide of Claim 4 wherein the serine/threonine kinase is from the Raf family and is selected from the group consisting of Raf-1, A-Raf and B-Raf.
- 10 6. The peptide of Claim 4 wherein the serine/threonine kinase is a G-protein dependent kinase selected from the group consisting of β 2-adrenergic receptor kinases, rhodopsin kinase and GRK4-6.
7. A peptide having the sequence of HJ-38 (SEQ ID NO.: 13), J-41 (SEQ ID NO.: 14), J-47 (SEQ ID NO.: 20), J-48 (SEQ ID NO.: 21), J-29 (SEQ ID NO.: 22), K014H010 (SEQ ID NO.: 63), K014H111 (SEQ ID NO.: 64), K048H901 (SEQ ID NO.: 66), K098H901 (SEQ ID NO.: 67), or K107H901 (SEQ ID NO.: 68).
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8. A peptide having the sequence of HJ-38 (SEQ ID NO.: 13), J-41 (SEQ ID NO.: 14), J-47 (SEQ ID NO.: 20), J-48 (SEQ ID NO.: 21), J-29 (SEQ ID NO.: 22), K014H010 (SEQ ID NO.: 63), K014H111 (SEQ ID NO.: 64), K048H901 (SEQ ID NO.: 66), K098H901 (SEQ ID NO.: 67), or K107H901 (SEQ ID NO.: 68), with the proviso that any one amino acid residue in the peptide can vary, being any naturally occurring amino acid or analog thereof.
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9. A peptide comprising a sequence of amino acids AA₁ through AA₂₀ or a subsequence thereof comprising at least five amino acids, wherein:
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AA₁ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

5 AA₂ is selected from the group consisting of glutamine, asparagine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₃ is selected from the group consisting of leucine, isoleucine, methionine and valine;

10 AA₄ is selected from the group consisting of leucine, isoleucine, methionine and valine;

AA₅ is selected from the group consisting of alanine, serine and threonine;

AA₆ is glycine or alanine;

15 AA₇ is selected from the group consisting of glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₈ is selected from the group consisting of leucine, isoleucine, methionine and valine;

AA₉ is proline;

20 AA₁₀ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

AA₁₁ is selected from the group consisting of alanine, serine and threonine;

25 AA₁₂ is selected from the group consisting of histidine, asparagine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₁₃ is selected from the group consisting of leucine, isoleucine, methionine and valine;

AA₁₄ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

5 AA₁₅ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

10 AA₁₆ is selected from the group consisting of arginine, N-nitroarginine, β -cycloarginine, γ -hydroxyarginine, N-amidinocitruline and 2-amino-4-guanidinobutanoic acid;

15 AA₁₇ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₁₈ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

20 AA₁₉ is selected from the group consisting of leucine, isoleucine, methionine and valine; and

AA₂₀ is selected from the group consisting of leucine, isoleucine, methionine and valine.

10. The peptide of Claim 9 wherein the sequence AA₁ through AA₂₀ or the
25 subsequence thereof corresponds to the sequence of the HJ loop of Raf (SEQ ID NO.: 1) or a subsequence thereof, with the proviso that any two amino acids in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.

11. The peptide of Claim 9 wherein the sequence AA₁ through AA₂₀ or the subsequence thereof corresponds to the sequence or a subsequence of the HJ loop of Raf (SEQ ID NO.: 1), with the proviso that any one amino acid in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.
- 5 12. The peptide of Claim 10 or Claim 11 wherein the peptide comprises an eight amino acid subsequence of the sequence A₁ through AA₂₀, wherein the subsequence is selected from the group consisting of AA₃ through AA₁₀, AA₇ through AA₁₄ and AA₁₁ through AA₁₈.
- 10 13. A peptide comprising a sequence of amino acids AA₁ through AA₂₀ or a subsequence thereof comprising at least five amino acids, wherein:
 - AA₁ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;
 - AA₂ is selected from the group consisting of glutamine, asparagine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or
 - 15 aspartic acid;
 - AA₃ is selected from the group consisting of leucine, isoleucine, methionine and valine;
 - AA₄ is alanine or glycine;
 - 20 AA₅ is selected from the group consisting of alanine, leucine, isoleucine, methionine and valine;
 - AA₆ is glycine or alanine;
 - AA₇ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;
 - 25 AA₈ is proline;
 - AA₉ is proline;

AA₁₀ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

AA₁₁ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

5 AA₁₂ is glycine or alanine;

AA₁₃ is selected from the group consisting of glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

10 AA₁₄ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₁₅ is proline;

15 AA₁₆ is selected from the group consisting of leucine, isoleucine, methionine and valine;

AA₁₇ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

20 AA₁₈ is selected from the group consisting of leucine, isoleucine, methionine and valine;

AA₁₉ is selected from the group consisting of tyrosine, phenylalanine and tryptophan; and

25 AA₂₀ is selected from the group consisting of glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid.

14. The peptide of Claim 13 wherein the sequence AA₁ through AA₂₀ or the subsequence thereof corresponds to the sequence of the HJ loop of cyclic AMP

dependent kinase (SEQ ID NO.: 2) or a subsequence thereof, with the proviso that any two amino acids in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.

15. The peptide of Claim 13 wherein the sequence AA₁ through AA₂₀ or the subsequence thereof corresponds to the sequence or a subsequence of the HJ loop of cyclic AMP dependent kinase (SEQ ID NO.: 2), with the proviso that any one amino acid in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.
16. The peptide of Claim 14 or Claim 15 wherein the peptide comprises an eight amino acid subsequence of the sequence A₁ through AA₂₀, wherein the subsequence is selected from the group consisting of AA₃ through AA₁₀, AA₇ through AA₁₄ and AA₁₁ through AA₁₈.
17. A peptide comprising a sequence of amino acids AA₁ through AA₂₀ or a subsequence thereof comprising at least five amino acids, wherein:

 - AA₁ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;
 - AA₂ is selected from the group consisting of glutamine, asparagine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;
 - AA₃ is selected from the group consisting of leucine, isoleucine, methionine and valine;
 - AA₄ is selected from the group consisting of leucine, isoleucine, methionine and valine;
 - AA₅ is selected from the group consisting of cysteine, alanine, leucine, isoleucine, methionine and valine;

AA₆ is glycine or alanine;

AA₇ is selected from the group consisting of histidine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

5 AA₈ is selected from the group consisting of proline, alanine and serine;

AA₉ is proline;

AA₁₀ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

10 AA₁₁ is selected from the group consisting of histidine, glutamine, asparagine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₁₂ is glycine or alanine;

15 AA₁₃ is selected from the group consisting of glutamine, asparagine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

20 AA₁₄ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

25 AA₁₅ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₁₆ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₁₇ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

5 AA₁₈ is selected from the group consisting of leucine, isoleucine, methionine and valine;

AA₁₉ is selected from the group consisting of tyrosine, phenylalanine and tryptophan; and

10 AA₂₀ is selected from the group consisting of histidine glutamic acid, and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid.

18. The peptide of Claim 17 wherein the sequence AA₁ through AA₂₀ or the subsequence thereof corresponds to the sequence of the HJ loop of protein kinase C (SEQ ID NO.: 3) or a subsequence thereof, with the proviso that any
15 two amino acids in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.

19. The peptide of Claim 17 wherein the sequence AA₁ through AA₂₀ or the subsequence thereof corresponds to a sequence or a subsequence of the HJ loop of protein kinase C (SEQ ID NO.: 3), with the proviso that any one amino acid
20 in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.

20. The peptide of Claim 18 or Claim 19 wherein the peptide comprises an eight amino acid subsequence of the sequence A₁ through AA₂₀, wherein the subsequence is selected from the group consisting of AA₃ through AA₁₀, AA₇ through AA₁₄ and AA₁₁ through AA₁₈.

21. A peptide comprising a sequence of amino acids AA₁ through AA₂₀ or a subsequence thereof comprising at least five amino acids, wherein:

AA₁ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

5 AA₂ is lysine or ornithine;

AA₃ is selected from the group consisting of leucine, isoleucine, methionine and valine;

AA₄ is selected from the group consisting of leucine, isoleucine, methionine and valine;

10 AA₅ is selected from the group consisting of arginine, N-nitroarginine, β-cycloarginine, γ-hydroxyarginine, amidinocitruline and 2-amino-4-guanidinobutanoic acid;

AA₆ is glycine or alanine;

AA₇ is histidine;

15 AA₈ is serine or threonine;

AA₉ is proline;

AA₁₀ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

20 AA₁₁ is selected from the group consisting of arginine, N-nitroarginine, β-cycloarginine, γ-hydroxyarginine, amidinocitruline and 2-amino-4-guanidinobutanoic acid;

AA₁₂ is selected from the group consisting of glutamine, asparagine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

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AA₁₃ is histidine;

AA₁₄ is lysine or ornithine;

AA₁₅ is serine or threonine;

AA₁₆ is lysine or ornithine;

AA₁₇ is selected from the group consisting of glutamine, asparagine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

5 AA₁₈ is lysine or ornithine;

 AA₁₉ is histidine; and

 AA₂₀ is selected from the group consisting of glutamine, asparagine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or
10 aspartic acid.

22. The peptide of Claim 21 wherein the sequence AA₁ through AA₂₀ or the subsequence thereof corresponds to the sequence of the HJ loop of bARK1.2 (SEQ ID NO.: 4) or a subsequence thereof, with the proviso that any two amino acids in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.

15 23. The peptide of Claim 21 wherein the sequence AA₁ through AA₂₀ or the subsequence thereof corresponds to the sequence or a subsequence of the HJ loop of bARK1.2 (SEQ ID NO.: 4), with the proviso that any one amino acid in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.

20 24. The peptide of Claim 22 or Claim 23 wherein the peptide comprises an eight amino acid subsequence of the sequence A₁ through AA₂₀, wherein the subsequence is selected from the group consisting of AA₃ through AA₁₀, AA₇ through AA₁₄ and AA₁₁ through AA₁₈.

25. A peptide comprising a sequence of amino acids AA₁ through AA₂₀ or a subsequence thereof comprising at least five amino acids, wherein:

AA₁ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

5 AA₂ is selected from the group consisting of glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₃ is selected from the group consisting of leucine, isoleucine, methionine and valine;

AA₄ is selected from the group consisting of leucine, isoleucine, methionine and valine;

10 AA₅ is selected from the group consisting of cysteine, serine and threonine;

AA₆ is glycine or alanine;

15 AA₇ is selected from the group consisting of arginine, N-nitroarginine, β -cycloarginine, γ -hydroxyarginine, N-amidinocitruline and 2-amino-4-guanidinobutanoic;

AA₈ is selected from the group consisting of leucine, isoleucine, methionine and valine;

AA₉ is proline;

20 AA₁₀ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

AA₁₁ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

AA₁₂ is asparagine or glutamine;

AA₁₃ is asparagine or glutamine;

25 AA₁₄ is selected from the group consisting of aspartic acid, glutamic acid and an aliphatic, substituted aliphatic, aromatic, substituted aromatic acid, benzylic or substituted benzylic ester of aspartic acid or glutamic acid;

AA₁₅ is selected from the group consisting of lysine, ornithine and histidine;

AA₁₆ is selected from the group consisting of asparatic acid, glutamic acid and an aliphatic, substituted aliphatic, aromatic, substituted aromatic acid, benzylic or substituted benzylic ester of aspartic acid or glutamic acid;

5 AA₁₇ is selected from the group consisting of arginine, N-nitroarginine, β -cycloarginine, γ -hydroxyarginine, N-amidinocitruline, 2-amino-4-guanidinobutanoic, lysine and ornithine;

AA₁₈ is selected from the group consisting of leucine, isoleucine, methionine and valine;

10 AA₁₉ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

AA₂₀ is selected from the group consisting of asparatic acid, glutamic acid and an aliphatic, substituted aliphatic, aromatic, substituted aromatic acid, benzylic or substituted benzylic ester of aspartic acid or glutamic acid.

26. The peptide of Claim 25 wherein the sequence AA₁ through AA₂₀ or the
15 subsequence thereof corresponds to the sequence of the HJ loop of Akt/PKB (SEQ ID NO.: 7) or a subsequence thereof, with the proviso that any two amino acids in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.
27. The peptide of Claim 25 wherein the sequence AA₁ through AA₂₀ or the
20 subsequence thereof corresponds to the sequence or a subsequence of the HJ loop of Akt/PKB (SEQ ID NO.: 7), with the proviso that any one amino acid in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.
28. The peptide of Claim 26 or Claim 27 wherein the peptide comprises an eight
25 amino acid subsequence of the sequence A₁ through AA₂₀, wherein the subsequence is selected from the group consisting of AA₃ through AA₁₀, AA₇ through AA₁₄ and AA₁₁ through AA₁₈.

29. A peptide comprising a sequence of amino acids AA₁ through AA₂₀ or a subsequence thereof comprising at least five amino acids, wherein:

AA₁ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

5 AA₂ is selected from the group consisting of leucine, isoleucine, methionine and valine;

AA₃ is selected from the group consisting of leucine, isoleucine, methionine and valine;

10 AA₄ is selected from the group consisting of leucine, isoleucine, methionine and valine;

AA₅ is selected from the group consisting of glutamine, leucine, isoleucine, methionine and valine;

AA₆ is glycine or alanine;

15 AA₇ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

AA₈ is proline;

AA₉ is proline;

AA₁₀ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

20 AA₁₁ is selected from the group consisting of tyrosine, phenylalanine and tryptophan;

25 AA₁₂ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₁₃ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₁₄ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

5 AA₁₅ is selected from the group consisting of asparagine, glutamine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₁₆ is histidine;

10 AA₁₇ is selected from the group consisting of arginine, N-nitroarginine, β -cycloarginine, γ -hydroxyarginine, amidinocitruline, 2-amino-4-guanidinobutanoic acid lysine and ornithine;

AA₁₈ is selected from the group consisting of lysine, ornithine, leucine, isoleucine, methionine and valine;

15 AA₁₉ is selected from the group consisting of tyrosine, phenylalanine and tryptophan; and

AA₂₀ is selected from the group consisting of glutamine, asparagine, glutamic acid, aspartic acid and an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid.

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30. The peptide of Claim 29 wherein the sequence AA₁ through AA₂₀ or the subsequence thereof corresponds to the sequence of the HJ loop of calmodulin dependent kinase (SEQ ID NO.: 5) or a subsequence thereof, with the proviso that any two amino acids in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.

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31. The peptide of Claim 29 wherein the sequence AA₁ through AA₂₀ or the subsequence thereof corresponds to the sequence or a subsequence of the HJ loop

of calmodulin dependent kinase (SEQ ID NO.: 5), with the proviso that any one amino acid in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.

32. The peptide of Claim 30 or Claim 31 wherein the peptide comprises an eight amino acid subsequence of the sequence A₁ through AA₂₀, wherein the subsequence is selected from the group consisting of AA₃ through AA₁₀, AA₇ through AA₁₄ and AA₁₁ through AA₁₈.
33. A peptide comprising a sequence of amino acids AA₁ through AA₂₀ or a subsequence thereof comprising at least five amino acids, wherein the sequence AA₁ through AA₂₀ or the subsequence thereof corresponds to the sequence of the HJ loop of polo (SEQ ID NO.: 6) or a subsequence thereof, with the proviso that any two amino acids in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.
34. A peptide comprising a sequence of amino acids AA₁ through AA₂₀ or a subsequence thereof comprising at least five amino acids, wherein the sequence AA₁ through AA₂₀ or the subsequence thereof corresponds to the sequence or a subsequence of the HJ loop of polo (SEQ ID NO.: 6), with the proviso that any one amino acid in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.
35. The peptide of Claim 33 or Claim 34, wherein the peptide comprises an eight amino acid subsequence of the sequence A₁ through AA₂₀, wherein the subsequence is selected from the group consisting of AA₃ through AA₁₀, AA₇ through AA₁₄ and AA₁₁ through AA₁₈.

36. A peptide comprising a sequence of amino acid residues AA₁ through AA₂₀ or a subsequence thereof comprising at least five amino acid residues, wherein:

AA₁ is alanine or glycine;

5 AA₂ is glutamic acid, aspartic acid or an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₃ is leucine, isoleucine, methionine or valine;

AA₄ is leucine, isoleucine, methionine or valine;

AA₅ is leucine, isoleucine, methionine or valine;

10 AA₆ is glycine or alanine;

AA₇ is asparagine or glutamine;

AA₈ is proline;

AA₉ is leucine, isoleucine, methionine or valine;

AA₁₀ is tyrosine, phenylalanine and tryptophan;

15 AA₁₁ is proline;

AA₁₂ is glycine or alanine;

AA₁₃ is aspartic acid, glutamic acid or an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of aspartic acid or glutamic acid;

20 AA₁₄ is serine or threonine;

AA₁₅ is glycine or alanine;

AA₁₆ is leucine, isoleucine, methionine or valine;

25 AA₁₇ is glutamic acid, aspartic acid or an aliphatic, substituted aliphatic, benzyl, substituted benzyl, aromatic or substituted aromatic ester of glutamic acid or aspartic acid;

AA₁₈ is asparagine or glutamate;

AA₁₉ is leucine, isoleucine, methionine or valine; and

AA₂₀ is leucine, isoleucine, methionine or valine.

37. The peptide of Claim 36, wherein the sequence AA₁ through AA₂₀ or the subsequence thereof corresponds to the sequence of the HJ loop of GSK3 (SEQ ID NO.: 12) or a subsequence thereof, with the proviso that any two amino acids in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.
- 5 38. The peptide of Claim 36, wherein the sequence AA₁ through AA₂₀ or the subsequence thereof corresponds to the sequence or a subsequence of the HJ loop of GSK3 (SEQ ID NO.: 12), with the proviso that any one amino acid in the sequence AA₁ through AA₂₀ or the subsequence thereof can vary.
- 10 39. The peptide of Claim 37 or Claim 38, wherein the peptide comprises an eight amino acid subsequence of the sequence A₁ through AA₂₀, wherein the subsequence is selected from the group consisting of AA₃ through AA₁₀, AA₇ through AA₁₄ and AA₁₁ through AA₁₈.
40. A method of identifying a peptide which modulates the activity of a serine/threonine kinase comprising the steps of:
- 15 a) providing a peptide, referred to as a "test peptide", comprising a peptide derivative of the HJ loop of said serine/threonine kinase and having from about five to about twenty amino acids or analogs thereof;
- b) incubating the test peptide with cells having one or more cellular activities controlled by a serine/threonine kinase under conditions suitable for assessing activity of the serine/threonine kinase;
- 20 c) assessing activity of the serine/threonine kinase, wherein greater or lesser activity compared with the cells grown without incubation of the test peptide indicates that the peptide modulates activity of the serine/threonine kinase.

41.
- The method of Claim 40, wherein the activity of the serine/threonine kinase is assessed by measuring the rate of survival or proliferation of said cells in tissue culture.
42.
- A method of modulating the activity of a serine/threonine kinase in a subject,
- 5
- comprising administering a therapeutically effective amount of a peptide comprising a peptide derivative of the HJ loop of a serine/threonine kinase, wherein:
- a)
- said peptide has between about five and about twenty amino acids or amino acid analogs; and
- 10
- b)
- said peptide modulates activity of the serine/threonine kinase.